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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/243,342	05/16/94	BUCALA	R 7613006

EXAMINER	
MOSELEY, A	
ART UNIT	**PAPER NUMBER**
1809	22

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DATE MAILED: 10/09/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

See the attached.

PTO-90C (Rev. 2/95)
*U.S. GPO: 1997-422-198/60031

1- File Copy

Office Action Summary	Application No. 08/243,342	Applicant(s) Bucala et al.
	Examiner Ardin Marschel	Group Art Unit 1809

☒ Responsive to communication(s) filed on 6/16/97 and IDS, filed 11/25/96.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 63, 80-82, and 84-90 is/are pending in the application.

~~Of the above~~, Claim(s) 1-62, 64-79, 83, and 90-93 have been canceled. ~~is/are withdrawn from consideration~~.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 63, 80-82, and 84-90 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892 ✓

☒ Information Disclosure Statement(s), PTO-1449, ~~Paper No(s).~~ 1 sheet ✓

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Applicants' arguments, filed 6/16/97, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because the specification contains sequences that fall under these rules without a SEQ ID NO. cited therewith. For example, on page 29, lines 18 and 21, sequences are cited without SEQ ID Nos. as required with such citations. Other sequences are given in the specification without SEQ ID NOs. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants have summarized antisense, ribozyme, and triple helix therapy in the specification on pages 44-49. Nowhere

therein, however, is there guidance as to what practice results in the specificity that has been amended into the claims. Specificity indicates that the therapy is directed to a specific site in a cell. This may be practiced by utilizing particular sequences, for example, in antisense oligonucleotides that hybridize only or specifically to MIF mRNA or other MIF nucleic acid in a cell. This suggests that such hybridization does not occur to other sites such as related mRNA or gene sequences. Consideration of the instant specification reveals that no such related sequence is disclosed by which to determine negative controls, for example. Without such negative controls, the practitioner in the art must devise some out of the myriad of sequences present in a cell. Human cells are known to contain tens of thousands, maybe as many as 100,000, gene sequences. Selection of appropriate negative controls such that antisense therapy, for example, is predictable is clearly undue experimentation without some guidance regarding negative controls. It is also known that hybridization conditions affect specificity regarding stringency. The conditions to utilize for designing antisense oligomers are also not instantly disclosed. It is completely guesswork, given the lack of instant guidance, to determine the required length and sequence of an antisense oligomer that would be effective. Stein et al. is cited as summarizing the multitude of factors that must be evaluated to result in effective antisense oligomers and that, in particular, specificity is difficult to obtain at best. See page 1006,

middle column, line 29, through page 1007, middle column, line 24. It is therein noted that some target nucleic acids are reasonably inhibited in one region such as the 3' untranslated region rather than the initiation codon or 5' cap region which is inhibited in other genes. It is also noted that the specificity of putatively sequence-specific oligos is in question as given on page 1007, first column, second full paragraph. There is no instant guidance as to what region or regions of the MIF sequence functions as a predictable target for either of antisense, ribozyme, or triple helix therapy.

Claims 63, 80-82, and 84-90 are rejected, as described above, under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 63, 80-82, and 84-90 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Abbreviations in claims are vague and indefinite unless followed by the full name so as to prevent confusion as to what is meant by the abbreviation. Applicants are requested to either replace MIF with its full name or insert its full name after each occurrence of this abbreviation.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 63, 80-82, and 84-90 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bernhagen et al.(ref. BU) taken in view of Uhlmann et al.(ref. BA) and Clark et al.(ref. CD).

Bernhagen et al. summarizes beneficial effects of inhibition of MIF action in inflammatory response in the abstract, for

example, in the treatment of septic shock. This motivates and suggests that inhibition of MIF activity is useful in the treatment of septic shock etc. but lacks disclosure of inhibition such as antisense therapy etc.

Uhlmann et al. is a generic summary document regarding the design and use of antisense therapy and reviews numerous parameters that must be considered in such a therapy but suggests and motivates the likely usefulness of this type of therapy. It is noted that Uhlmann et al. also describes ribozyme and triple helix therapy on pages 574-575. Such therapy needs sequence information of the gene or mRNA to be inhibited.

Clark et al. discloses the sequencing of MIF and thus supplies the sequence information needed for the Uhlmann et al. methodology.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention because Bernhagen et al. suggests and motivates the usefulness of MIF inhibition type therapy, Uhlmann et al. supplies such a therapy to inhibit a gene product activity of which MIF activity is one, and Clark et al. supplies the required sequence information to utilize in the Uhlmann et al. therapeutic method. The combination of references therefore both motivates and suggests the instant invention and supplies the information needed to practice it. It is noted that the guidance in this combination of references is the same as in the instant disclosure in that generic methods of therapy are instantly

summarized for antisense therapy without detailed MIF sequence analysis connected with this gene or mRNA. Therefore, the combination of references cited in support of this rejection supplies the same level of knowledge regarding this therapy as does the instant disclosure and is rejected on this basis.

No claim is allowed.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

September 30, 1997

Ardin H. Marschel

ARDIN H. MARSCHEL
PRIMARY EXAMINER
GROUP 1800